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EFFECTIVENESS OF IMMUNIZATION AGAINST INFLUENZA OF TISSUE VACCINE OF THE INSTITUTE OF VIROLOGY OF THE ACADEMY OF MEDICAL SCIENCES USSR

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A vaccination was conducted in December 1953 in Leninaka (Armenian SSR) against virus influenza by tissue vaccine of the Institute of Virology AMN SSSR [Akademiya Meditsinskikh Nauk -- Academy of Medical Sciences USSR] which had been proposed by V. M. Zhdanov. The tissue polyvaccine included viruses of the 3 types -- A, A_1 and B.

We diluted the dry vaccine in physiological saline solution before using it, calculating one cc of solution for each dose of the preparation; it was inoculated in the diluted form into the nasal passages of the subject by means of a pulverizer. Each person inoculated received one dose of the vaccine.

The vaccination was conducted among workers and clerks of one weaving and 2 spinning mills in Leninakan; in all 3,516 persons were vaccinated. One group of workers of the spinning mill and one of the stocking knitwear factory, in all 3,640 persons, served as control groups. The inoculations were conducted simultaneously in the period from 13 through 26 December 1953.

In those vaccinated there was observed a constitutional reaction in the form of elevated temperature, catarrhal signs in the respiratory tracts, headaches, etc. Of 3,516 vaccinated, elevation of temperature was noted in 42 persons (1.2%), catarrhal signs of the mucus membranes of the upper respiratory tracts in 263 (7.5%), headaches in 186 (5.3%), and general malaise in 95 persons (2.7%). All of the signs mentioned above were brief in the majority of those inoculated and lasted less than a day.

Eleven of those inoculated were on the sick list from one to 3 days.

With the aim of clarifying the epidemiological effectiveness of the vaccination we conducted an observation from 5 January to 25 May 1954 on the morbidity rate with influenza and colds of those vaccinated and those not vaccinated. A special card was kept on each person; it contained all the necessary data, including the date of inoculation type and series of vaccination, reaction after vaccination, and, for those who became ill, also the time of illness, duration of inability to work, and results of serological investigations. We kept a special account of all patients who were registered by physicians as becoming ill with influenza and colds and obtained the sick lists.

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The morbidity due to influenza and colds for the period covering the observations was 2.8%, among those vaccinated and 8.5% among those not vaccinated, that is, the morbidity in the first group dropped by 3.04 times (Table 1). The average duration of inability to work of patients among those inoculated equalled 4.9 days; for those not inoculated 5.55 days, that is, in the first case it was on the average 0.65 days less.

TABLE 1

MORBIDITY RATE DUE TO INFLUENZA AND COLDS AND LOSS OF WORK DAYS AMONG THOSE IMMUNIZED AND THOSE NOT IMMUNIZED

Influenza	Number under observation	Individuals ill with influenza and colds		Number of work days lost	Average duration of patients' inability to work (days)
		number	%		
Immunized	3,516	98	2.8	483	4.9
Nonimmunized	3,640	307	8.5	1,704	5.55

With the aim of differential diagnosis of influenza and colds the sera obtained from the patients at the onset of the disease (in the first 2-4 days) and after recovery (after 15-20 days) were subjected to examination by means of the reaction of inhibition of hemagglutination. We performed the reaction with a 2% suspension of chick erythrocytes.

In all the serum of 377 patients was investigated (immunized and nonimmunized). Of them 201 were registered in the polyclinic with the diagnosis "virus influenza" and 176 with the diagnosis "cold."

TABLE 2

RESULT OF THE REACTION OF HEMAGGLUTINATION INHIBITION IN PATIENTS STUDIED

Polyclinic diagnosis	Number studied	Result of investigation				Number of Times antibody titer increased					
		No increase in titer noted		Titer of antibodies increased							
		number	%	number	%	2 times	4 times	8 times	16 times	32 times	64 times
Virus influenza	201	35	17.5	166	82.5	27	37	71	23	7	1
Cold	176	84	47.7	92	52.3	13	20	41	14	3	1
Total	377	119	-	258	68.4	40	57	112	37	10	2

A positive result, that is, an increase of antiinfluenza antibodies, was noted in 166 (82.5%) of patients with the diagnosis "influenza" and in 92 (52.3%) of patients with the diagnosis "cold." Thus in the study of 377 patients the increase of titer of antiinfluenza antibodies occurred in 258, that is, in 68.4% of patients.

Of 258 positive cases, increase of titer of antibodies to the virus type A was noted in 175 (67.8%), to virus type B, in 17 (6.6%), to type A_1, in 59 (22.9%) of patients. The high percentages of increase of titer

of antibodies to the virus Type A has first been noticed by us for the past 3 years. In 7 patients an increase of antiinfluenza antibodies was recorded to all 3 types.

Aside from the above, we investigated the blood of 21 patients (of the immunized as well as the nonimmunized group) only once on the fifteenth to thirtieth day after the onset of the disease. The diagnosis "influenza" was made in 12 of them, while in 9 the diagnosis of "cold." In 2 the antibody titer equalled 1:320; in 6, 1:160; in 5, 1:80; in the rest it was lower. We could not get blood from 7 patients.

Thus of 405 convalescents we managed to investigate 398 patients, a positive result was obtained in 271 of them, of 68.4% of all patients studied.

With the aim of establishing the immunogenicity of the antiinfluenza tissue vaccine in the 391 inoculated, we investigated the blood before and within 15-20 days after the vaccination by means of the same hemagglutination reaction with 2% suspension of chick erythrocytes. An increase of virus-neutralizing antibodies was noted in 351, that is, 89.8% of all those examined. With this the titer increased by 2 times in 13.9% of those inoculated, by 4 times in 48.4%, by 8 times in 27.9%, by 16 times in 5.9%, by 32 times in 5.3%, and by 64 times in 3 of those inoculated or 0.8%.

Despite the fact that the vaccinations were conducted with polyvaccine, the titer was not the same with respect to the individual components of the vaccine: in 64.4% there was noted a shift of antibodies for type A; in 19.7% for type B; in 14.8% for type A_1; in 4 of those inoculated (1.1%) there was noted an increase of titer to 2 or 3 types of virus (Table 3).

TABLE 3

RESULTS OF SEROLOGICAL INVESTIGATION BEFORE AND AFTER VACCINATION ACCORDING TO VIRUS TYPES

Number investigated	Number of cases of increase of titer		Analysis with Respect to Type							
			A		A_1		B		Group reaction	
	No	%	No	%	No	%	No	%	No	%
391	351	89.8	226	64.4	52	14.8	69	19.7	4	1.1

The data obtained attest to the notable increase in the titer of antiinfluenza antibodies in the blood after vaccination; this also speaks for the considerable effectiveness of immunization by tissue vaccine.

The question as to the period of preservation of the immunity by those inoculated is also of great interest. To clarify this we studied in those persons the changes of titer of virus-neutralizing antibodies after 2-1/2, 4, and 6-1/2 months. In this manner 348 were included in a 3-fold examination, 313, in a 4-fold and 308, in a 5-fold investigation.

The data obtained (Table 4) showed that the degree of postvaccinal immunity falls in those inoculated with the passage of time: if after 15-20 days following the vaccination the percentage of positive cases was 89.8%, then after 2-1/2 months it fell to 66.1, after 4 months to 53.7 and after 6-1/2 months to 25%.

TABLE 4

CHANGES IN TITER OF ANTIINFLUENZA ANTIBODIES IN THOSE INOCULATED AFTER 15 DAYS AND 2-1/2, 4, AND 6-1/2 MONTHS

Time between Inoculation and Examination	No of persons examined	No of those inoculated in whom an increase of titer was noted		Multiple of Increase in Antibody Titer											
				2 times		4 times		8 times		16 times		32 times		64 times	
		No	%	No	%	No	%	No	%	No	%	No	%	No	%
15 days	331	351	89.8	49	14	161	45.9	98	27.9	21	5.9	19	5.4	3	0.9
2-1/2 months	348	230	66.1	63	27.4	102	44.35	49	21.3	7	3	8	3.55	1	0.4
4 months	313	168	53.7	68	40.5	66	39.2	26	15.5	4	2.4	4	2.4	-	-
6-1/2 months	308	77	25	49	63.7	18	23.4	7	9.1	1	1.3	1	1.3	1	1.3

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Thus, after the intranasal vaccination of tissue vaccine, the titer of antiinfluenza antibodies was preserved in the majority of the inoculated for a period of 2-1/2 to 4 months in not less than 50% of those inoculated.

Conclusions

1. Intranasal injection of tissue vaccine (Zhdanov) evoked a mild local as well as general reaction in 17% of those inoculated. The reaction occurred during the initial hours after vaccination and continued less than a day.

2. The tissue vaccine possesses manifest immunogenic properties: it conditioned a drop of morbidity due to influenza among those inoculated by 3.04 times in comparison to those not inoculated.

3. With the intranasal introduction of tissue vaccine in the majority of those inoculated, we observed an increase of antiinfluenza antibodies which were still detected after 6-1/2 months in 25% of those inoculated.

4. Analysis of the epidemiological and immunological data showed that tissue vaccine is sufficiently effective for its utilization in the capacity of a means of specific prophylaxis against virus influenza.

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